NCI Physical Sciences-Oncology Centers (PS-OC) Program
Strategic Workshop

Applying Physical Sciences Perspectives from Developmental Biology and Tissue Engineering to Cancer Research

Executive Summary, Agenda, and Participants List

April 25, 2012

The Cloisters, Building 60
National Institutes of Health Campus
Bethesda, Maryland

Office of Physical Sciences-Oncology
National Cancer Institute
National Institutes of Health
U.S. Department of Health and Human Services

Executive Summary

The National Cancer Institute (NCI) Office of Physical Sciences – Oncology (OPSO) launched the Physical Sciences – Oncology Centers (PS-OC) Program in 2009 to complement our current understanding of cancer by forming teams of physical scientists and cancer researchers working together to bring a novel “physical sciences perspective” to cancer biology. In February 2012, OPSO held a Think Tank meeting to reflect on program progress and to identify additional areas where physical sciences perspectives could inform our understanding of cancer. Think Tank participants evaluated current topics being investigated in the PS-OC Program and explored potential future areas of emphasis. One recommendation that emerged from the Think Tank was the exploration of links between cancer and development or tissue regeneration using a physical sciences perspective to potentially provide additional insight into our understanding of cancer. The physical forces involved in tumor initiation and metastasis are currently being studied in the PS-OC Program, and it was discussed that this thematic area might benefit, expand, and strengthen its basis with insights from developmental biology and tissue engineering and regenerative medicine. Bringing together experts from the scientific community, OPSO convened a Strategic Workshop in April 2012 titled “Applying Physical Sciences Perspectives from Developmental Biology and Tissue Engineering to Cancer Research” to explore areas where physical sciences perspectives from developmental biology and tissue engineering could open new avenues in cancer research.

Participants in this Strategic Workshop included researchers from the fields of developmental biology, tissue engineering and regenerative medicine, bioengineering, chemical engineering, chemistry, computational physics, and cancer research. Their wide range of expertise set the tone for the transdisciplinary nature of the discussion topics. With the premise that cancer is a complex disease that should be examined as a dynamic system across all length and time scales, participants explored whether lessons learned from understanding how gradients of chemical factors and physical forces are required to coordinate the shaping and patterning during embryogenesis and tissue formation could be applied to cancer. Presentations, roundtable discussions, and brainstorming sessions were used to determine if the state of the art physical sciences perspectives being brought to bear in developmental biology and tissue engineering could be used to address critical questions concerning cancer initiation, progression, and metastasis across length and time scales.

Key findings presented and ideas generated by workshop participants included:

Mechanical modules in cancer development

- Pulling and pushing among cells occurs during tissue development and the interplay between these two competing forces is critical for maintaining proper developmental programs as well as during epithelial to mesenchymal transition in cancer. Mechanical factors that may be involved in normal development and in emergent properties of cancer should be examined in the context of differences in how signals are propagated both mechanistically and at different length and time scales. Going forward, it may be informative to adopt tools and approaches from developmental biology and tissue engineering to further understand the role that mechanics plays in information transfer from the cell nucleus to tissue and back during cancer progression.
- Computational physics approaches suggest that adhesive forces between cells are one example of an “order parameter” (*i.e.*, a variable that has nonlinear behavior) that can correct developmental mistakes, and a breakdown in normal adhesion can trigger abnormal differentiation and neovascularization. Such results demonstrate that it is critically important to understand the

boundary conditions between a tumor and the microenvironment to define the “state space” (*i.e.*, an abstract space used to define the behavior of a system) of cancer from a set of physical sciences-based “order parameters.” This effort will require generating data related to the physical and mechanical forces operating at the cell-cell and cell-matrix boundaries.

Developing a synthetic human oncology

- The field of tissue engineering and regenerative medicine has made advances in developing “synthetic” *in vitro* and *ex vivo* model systems to recreate tissues and their microenvironment. Specific areas of advancement are the use of decellularized tissues and microfluidics platforms to create tissue model systems that closely resemble *in vivo* structure and function. The application and advancement of “synthetic” human oncology models that use tissue engineering technologies and approaches could be used to better mimic *in vivo* conditions and more precisely control experimental variables, such as spatial, molecular, and physical information entering the system.
- Cancer is a disease of both cells and organs. The physical sciences excel at integrating across scales, and thus may help in bridging these length scales. The key will be developing enough information at the organ level to enable physical scientists to build bridges to the cellular level.

Tumor dynamics and evolution

- Computational physics approaches are reaching a level of sophistication and power that enable them to be useful for modeling and understanding the dynamics of tumor differentiation. Analytical methods should be developed for assessing the emergent properties of multiple cells and tissues and to study cancer as an evolution of social interactions between cell populations.
- Studies on developmental dynamics are now possible because of the successful efforts at growing stem cells in culture to produce differentiated tissues under controlled conditions and the concomitant development of imaging techniques that can track single cells in living embryos in real time. Whole-tissue live imaging methods used to track differentiation and migration at the single-cell level could be useful for studying both the development of tumors in three dimensions and the interactions between tumor and co-cultured stroma either *in vivo* or *in vitro* in real time. Imaging analysis results could provide insight for identifying the order parameters of tumor systems predicted by computational physics approaches that are used to study tumor dynamics and evolution.
- The spatial-temporal relationships of exogenous signals expressed during development have been modeled computationally to understand the wave propagations of signals and the importance of patterns in protein expression levels. The study of relevant patterned signals in cancer could potentially yield new insight in cancer progression.

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Application of Physical Sciences Perspectives From
Developmental Biology and Tissue Engineering to Cancer Research

April 25, 2012

The Chapel in Building 60
National Institutes of Health
Bethesda, Maryland

Agenda

Meeting Objectives

The NCI's goal in this strategic workshop is to explore the research opportunities at the intersection of the physical sciences and cancer biology by bringing physical sciences perspectives from developmental biology and tissue engineering to enable a deeper understanding of cancer and inform better approaches to detect, treat and prevent this complex disease.

From the perspective of both the physical and biological sciences the strategic workshop aims are to:

- Determine the "state of the science" in developmental biology and tissue engineering at the level of physical forces, dynamics of pattern development, and advancing technologies and their application to cancer research at all scales.
- Identify specific critical questions in cancer research that can benefit from physical sciences perspectives that have been applied in developmental biology and tissue engineering that, if addressed, will enhance our understanding of cancer development, progression and metastasis at all scales.
- Offer guidance on how, through leadership and utilization of existing and new research support mechanisms, the NCI can best engage broader communities of developmental biologists and tissue engineers to address key questions in cancer research.

Outcomes

The conversations that comprise this strategic workshop, including brainstorming sessions, presentations, roundtable discussions, and reports from breakout groups, will be captured in a report that will be available on the NCI Office of Physical Sciences – Oncology website. In addition, input from the meeting will be utilized to inform new research directions and mechanisms that will hopefully energize and advance this critical field.

Synopsis

Cancer is a complex disease that must be examined as a dynamic system across all time and length scales. Similarly, the development of a multicellular organism is a well-orchestrated biological process that requires an exquisite spatio-temporal series of events. Gradients of chemicals and physical forces are required to coordinate the shaping and patterning that occurs during embryogenesis. Indeed, because of the misregulation of pathways employed during development, cancer is often described as development gone awry. Understanding these processes in the context of tissue development is also vital for tissue engineering, where model systems are created to generate functional tissues. The mission of the NCI Office of Physical Sciences – Oncology is to explore new and innovative approaches to better understand and control cancer by enabling the convergence of the physical sciences with cancer biology. To explore the areas where physical sciences perspectives from developmental biology and tissue engineering could be applied to cancer research, the NCI Office of Physical Sciences – Oncology will convene a meeting of experts from these different arenas at this strategic workshop to identify key questions and approaches that could open new avenues in cancer research.

8:00 a.m. - 8:15 a.m.	Introduction to the Strategic Workshop Nastaran Z. Kuhn, Ph.D. Project Manager Office of Physical Sciences - Oncology National Cancer Institute, NIH	*Chapel*
8:15 a.m. - 8:55 a.m.	Keynote Presentation *Physical Sciences Perspectives from Developmental Biology and Tissue Engineering* Yoshiki Sasai, M.D., Ph.D. Director of Neurogenesis and Organogenesis Group RIKEN Center for Developmental Biology	
8:55 a.m. - 9:45 a.m.	Roundtable Discussions	
9:45 a.m. - 10:15 a.m.	Keynote Presentation *Forces in Tissue Morphogenesis and Embryogenesis* Raymond E. Keller, Ph.D. Professor of Biology University of Virginia	
10:15 a.m. - 10:45 a.m.	Discussion Moderator: Jan Liphardt, Ph.D. Associate Professor of Physics Director of University of California, Berkeley Physical Sciences – Oncology Center University of California, Berkeley	
10:45 a.m. - 11:00 a.m.	Break	
11:00 a.m. - 11:30 a.m.	Panel Presentations: *Dynamics of Pattern Development* James A. Glazier, Ph.D.	

	Professor of Physics Director of Biocomplexity Institute Indiana University Anna-Katerina Hadjantonakis, Ph.D. Associate Member Memorial Sloan-Kettering Cancer Center Darryl Shibata, M.D. Professor of Medicine University of Southern California	
11:30 a.m. - 12 noon	Discussion Moderator: Thea D. Tlsty, Ph.D. Professor of Pathology Director of Center for Translational Research in the Molecular Genetics of Cancer University of California, San Francisco	
12 noon - 12:25 p.m.	Break to Serve Lunch Working Lunch	
12:25 p.m. - 12:55 p.m.	Keynote Presentation *Advancing Technologies From Developmental Biology and Tissue Engineering* George M. Whitesides, Ph.D. Woodford L. and Ann A. Flowers University Professor of Chemistry Harvard University	
12:55 p.m. - 1:25 p.m.	Discussion Moderator: Robert H. Austin, Ph.D. Professor of Physics Director of Princeton University Physical Sciences – Oncology Center Princeton University	
1:25 p.m. - 2:15 p.m.	Roundtable Discussions	
2:15 p.m. - 2:30 p.m.	Break	
2:30 p.m. - 3:45 p.m.	Breakout Sessions	*Chapel, Lecture Hall, and Classroom*
3:45 pm - 4:45 pm	Report Out From Breakout Sessions	*Chapel*
4:45 p.m. - 5:00 p.m.	Summary and Next Steps Nastaran Z. Kuhn, Ph.D. Project Manager Office of Physical Sciences – Oncology National Cancer Institute, NIH	

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